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Guidance for Industry

Special Control Guidance for Premarket Notifications for Totally Implanted Spinal Cord Stimulators for Pain Relief

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**U.S. Department of Health and Human Services
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**Restorative Devices Branch
Division of General, Restorative, and Neurological Devices
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Preface

Public Comment:

For 30 days following the date of publication in the Federal Register of the notice announcing the availability of this guidance, comments and suggestions regarding this document should be submitted to the Docket No. assigned to that notice, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852.

Additional Copies:

Additional copies are available from the Internet at: [http://www.fda.gov/cdrh/\[specific address\]](http://www.fda.gov/cdrh/[specific address]), or CDRH Facts on Demand. In order to receive the, "Special Control Document for Premarket Notifications for Totally Implanted Spinal Cord Stimulators for Pain Relief" via your fax machine, call the CDRH Facts-On-Demand system at 800-899-0381 or 301-827-0111 from a touch-tone telephone. Press 1 to enter the system. At the second voice prompt press 1 to order a document. Enter the document number 1179 followed by the pound sign (#). Follow the remaining voice prompts to complete your request."

Special Control Guidance¹ for Premarket Notifications for Totally Implanted Spinal Cord Stimulators for Pain Relief

Introduction

This document provides sponsors and FDA staff with guidance for totally implanted spinal cord stimulators (SCSs) for pain relief for premarket notifications [510(k)s]. This document identifies administrative, descriptive, and technical information that should be included in a 510(k) submission for totally implanted SCS devices for pain relief. Individual 510(k) submissions may need additional information pertinent to each specific device. Use of this document in the preparation of a 510(k) will help ensure that sufficient information is available for a substantive review of a SCS 510(k) submission. Manufacturers should comply with either the recommendations of this guidance or some alternate means that provide equivalent assurance of safety and effectiveness.

All FDA publications referred to in this guidance document can be obtained by contacting the Division of Small Manufacturers Assistance (DSMA) at 800-638-2041 (toll free) or 301-443-6597. Some FDA publications can be obtained via DSMA's Internet site at www.fda.gov/cdrh/dsmamain.html.

¹This document is intended to provide guidance. It represents the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Additional Sources Of Information

Full-text searches of the Code of Federal Regulations (CFR) can be accessed online by entering the CFR title, part and section numbers, e.g., 21 CFR 807.87, into the online database at: <http://www.access.gpo.gov/nara/cfr/cfr-retrieve.html#page1>

Questions or comments regarding this online CFR database service should be directed to the Government Printing Office (GPO) Access User Support Team by Internet e-mail at gpoaccess@gpo.gov; by telephone at (202) 512-1530 or (888) 293-6498 (toll free); or by fax at (202) 512-1262.

Additional specific topics relating to medical device regulations, policies, and guidance can be accessed under the alphabetical Topic Index on the CDRH home page located at: <http://www.fda.gov/cdrh>

510(k) Submission Content

Any 510(k) submitted under premarket notification procedures described in 21 CFR Part 807, Subpart E, for FDA's determination that the new device is substantially equivalent to a legally-marketed predicate (existing) device identified as a totally implanted spinal cord stimulator for pain relief should follow the format below and should contain all specified information that is applicable to the device.

A description of general information to be contained in each premarket notification submission is described in 21 CFR 807.87. Additional information relating specifically to premarket notifications can be accessed at: <http://www.fda.gov/cdrh> by searching in the Topic Index under "P" for Premarket Notification.

In addition, a copy of the 510(k) manual entitled, "Premarket Notification: 510(k) - Regulatory Requirements for Medical Devices" (HHS Publication FDA 95-4158) can be obtained by contacting DSMA, or via Internet at: <http://www.fda.gov/cdrh/manual/510kp1.html>

Administrative and General Information

The sponsor should provide the following administrative and general information:

1. Table of contents and continuous pagination of the submission and all appendices or attachments;
2. Name and address of both the device manufacturer and sponsor of the 510(k) submission;

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3. Identification of the official contact person, including address and telephone number, for all correspondence;
4. Sponsor's FDA establishment registration number, if available;
5. Proprietary name of the device, including name and model number, if applicable;
6. Generic name (and/or classification name) of the device, e.g., totally implanted spinal cord stimulator;
7. Panel code and product code for the device;
8. Proposed regulatory class for the new device, e.g., Class II;
9. Identification of the legally-marketed predicate device to which substantial equivalence is claimed;
10. Classification of the predicate device, e.g., Class II;
11. Information on whether the proposed device:
 - a. Has been previously submitted to the FDA for the same or different indications;
 - b. Is currently being reviewed for different indications within ODE; or
 - c. Was previously cleared by the FDA for different indications;
12. Actions taken to comply with the requirements of section 514 of the act, regarding compliance with applicable performance standards, in accordance with 21 CFR 807.87(d);
13. "510(k) Summary" as described in 21 CFR 807.92 or a "510(k) Statement" as described in 21 CFR 807.93, in accordance with 21 CFR 807.87(h);
14. 510(k) submissions with clinical data or referring to clinical data should include a financial certification or disclosure statement (applicable to all 510(k) submissions containing references to clinical study data), in accordance with 21 CFR 807.87(i);
15. "Truthful and Accurate Statement" signed by a responsible person of the firm required to submit the premarket notification, in accordance with 21 CFR 807.87(k); and
16. "Indications for Use" statement enclosure on a separate sheet of paper that lists the device name and clearly identifies the specific indications for use for which a determination of substantial equivalence is sought.

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Descriptive Information

Intended Use and Indications for Use

The sponsor should identify and describe the proposed intended use of the device.

Labeling

The sponsor should provide a complete copy of all labels, labeling, as well as all available promotional and advertising materials. Attachment I contains additional guidance concerning labeling of totally implanted SCSs.

Device Description

The sponsor should provide a complete description of the proposed device and accessories and a comparison to the legally-marketed predicate device. This description and comparison should include the following information:

1. Written description of the proposed device, including all device accessories, and any new features of the device;
2. Identification of the dimensions and weight of the device and accessories;
3. Description of all user controls, displays, and functions;
4. Description of device interconnections with other components;
5. Engineering drawings and/or photographs of the device; and
6. Detailed side-by-side comparison table of the relevant features and specifications of the proposed and predicate devices. This comparison table should be accompanied by a discussion of all similarities and differences between the devices and should be sufficiently detailed to provide a basis for a potential determination of substantial equivalence.

Additional descriptive information specific to totally implanted SCS devices should be provided. Please refer to Attachment II for guidance concerning the recommended content and format for reporting technological characteristics.

Attachments

Attachment I: Labeling

Attachment II: Technological Reporting

Attachment III: Device Testing and Manufacturing

Attachment I

Labeling

General Labeling Guidance

General labeling requirements for medical devices are described in 21 CFR Part 801. Proposed labels, labeling, advertising and/or promotional materials, and specifications sufficient to describe the device, its intended use and directions for use should be provided.

Copies of the following labeling guidance documents may be obtained from DSMA at 1-800-638-2041, or copies may be obtained via the Internet at the following addresses:

ODE Bluebook Memo G91-1, "Device Labeling Guidance," dated March 8, 1991:
<http://www.fda.gov/cdrh/g91-1.html>

"Medical Device Labeling: Suggested Format and Content," dated April 25, 1997:
<http://www.fda.gov/cdrh/ode/labeling.pdf>

"Labeling: Regulatory Requirements for Medical Devices," HHS Publication number FDA 89-4203, dated August, 1989:
<http://www.fda.gov/cdrh/dsma/470.pdf>

Specific Labeling Guidance for Totally Implanted SCSs

Prescription Statement

Totally implanted SCSs are prescription devices. Prescription devices must be labeled in accordance with 21 CFR 801.109.

User Manuals

User manuals should be provided for physician use and patient use. In addition to the prescription statement described above, a manual should include the following information:

1. Description of the device and its accessories;
2. Illustrations of the device and its accessories;
3. Description of all features, functions, output modalities, and specifications;
4. Description of all user-accessible controls;

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5. Indicators, markings, and/or labels on the device and accessories which provide information regarding the function or meaning of each control, display, output jack, etc.;
6. Directions for cleaning and/or maintenance where appropriate;
7. Storage and sterilization information;
8. Statements of indications, contraindications, warnings, precautions, and adverse reactions, as described in detail below; and
9. The physician manual should include instructions for correctly implanting, testing, using, and explanting the device.
10. A separate user manual for the patient in lay language should be provided.

The remainder of this labeling attachment lists statements that should be included prominently in the labeling for totally implanted spinal cord stimulators. These statements address the indications, contraindications, warnings, precautions, and adverse effects associated with the use of totally implanted spinal cord stimulators.

Indications for Use

Totally implanted SCSs are indicated for use as an aid in the management of chronic, intractable pain of the trunk or limbs.

Life Table

A chart illustrating the estimated service life (i.e., battery life) of the device at various output usages should be provided.

Shelf Life

For all implanted life-limiting components, a statement as to shelf life should be included on the labeling.

Contraindications

The contraindications should specifically address those patients who fail to receive pain relief during test stimulation.

Warnings

The warnings should specifically address the following:

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1. Use of totally implanted SCS devices in patients with cardiac demand pacemakers;
2. Safety of totally implanted SCS devices for use during pregnancy;
3. Effects of postural changes on totally implanted SCS devices;
4. Burns that may result if the generator case is ruptured or pierced; and
5. Effects of external sources of electromagnetic interference (EMI) devices on totally implanted SCS devices. All adverse effects that have been determined from electromagnetic compatibility (EMC) testing should be included in this warning.

Precautions

The precautions should specifically address the following:

1. Effects from the operation of other implanted medical devices on totally implanted SCS devices;
2. Effects of high output ultrasonic devices, radiation therapy, diathermy devices and external defibrillation devices on totally implanted SCS devices; and
3. Magnetic resonance imaging (MRI) compatibility issues.

Adverse Effects

The labeling should list the following risks associated with use of totally implanted SCS devices and the surgical implantation procedures:

1. Lead migration, which can result in changes in stimulation and subsequent reduction in pain relief;
2. Device failure, including battery failure, lead breakage, hardware malfunction, and loose connections which can lessen or eliminate stimulation and can result in ineffective pain control;
3. Adverse tissue reaction due in part to biocompatibility concerns;
4. Skin erosion over the IPG;
5. Surgical procedural risks, including temporary pain at the implant site, infection, cerebrospinal fluid (CSF) leakage and although rare, epidural hemorrhage, seroma, hematoma, and paralysis;
6. External sources of electromagnetic interference may cause the device to malfunction and may change stimulation parameters;

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7. If the device is not MRI compatible, adverse consequences can result, including heating of tissue, image artifacts, induced voltages in the IPG and/or leads, or dislodgment.

Attachment II

Technological Reporting

Introduction

This attachment provides guidance regarding information that should be included in a 510(k) submission for a totally implanted SCS in order to document the technological characteristics of the new device and to compare its characteristics to those of the identified legally-marketed predicate device. The documentation that should be provided includes the following:

- Section 1: Pulse Generator Output Specifications
- Section 2: Lead, Electrode, Programmer and Battery Descriptions
- Section 3: Description of Accessories
- Section 4: Description of Software/Firmware/Microprocessor Control

In addition, the submission should include a description of all similarities and differences between the new device and the predicate device. Ideally, the submission should also contain a table or tables that compare the Basic Unit Characteristics and Output Specifications of the two devices, as outlined in sections 2 and 3 of this attachment.

Section 1: Pulse Generator Output Specifications

An output mode is defined (for reporting purposes) as a version of a waveform produced by the unit. For example, biphasic symmetrical, biphasic asymmetrical and monophasic would all be considered separate output modes. A copy of the following information should be completed for each output mode. If a specific parameter is not applicable (N/A), this should be noted.

	<u>New Device</u>	<u>Predicate Device</u>
510(k) Number	(To Be Assigned)	K _____
Device Name, Model	_____	_____
Manufacturer	_____	_____
Number of Output Channels	_____	_____
- Synchronous or alternating?		
- Method of channel isolation?		

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Waveform (e.g., biphasic)	_____	_____
Shape (e.g., rectangular, sinusoidal)	_____	_____
Maximum Output Voltage (specify units) (+/- _____ %)	[voltage should be reported at a range of 300 to 2000 Ω]	
Maximum Output Current (specify units) (+/- _____ %)	[current should be reported at a range of 300 to 2000 Ω]	
Pulse Width (specify units)	_____	_____
Frequency (Hz)	_____	_____
For multiphasic waveforms:		
- Symmetrical phases?	Yes / No	Yes / No
- Phase Duration (include units) (state range, if applicable) (both phases, if asymmetrical)	_____	_____
Net Charge (μC per pulse) (should be zero)	_____ @ 500 Ω	_____ @ 500 Ω
Maximum Phase Charge (μC)	_____ @ 500 Ω	_____ @ 500 Ω
Maximum Current Density (mA/cm^2)	_____ @ 500 Ω	_____ @ 500 Ω
Maximum Power Density (W/cm^2)	_____ @ 500 Ω	_____ @ 500 Ω
ON Time (seconds)	_____	_____
OFF Time (seconds)	_____	_____
Additional Features, if applicable		

Notes:

Variable Parameters: For continuously variable parameters, specify the full range; for parameters with discrete settings, specify all available selections.

Density Measurements: Maximum current density and power density values should be calculated using the conductive surface area of the smallest electrode provided/recommended

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for use with the unit; sample calculations should be provided. The maximum power density should be based on the maximum duty cycle and should be averaged over an appropriate time frame.

Test Stimulation

If a trial period of epidural test stimulation is conducted, the sponsor should ensure that the stimulating equipment provided, e.g., test stimulator, for the test and the implanted device are capable of producing the same parameters. If they are not capable of producing the same parameters, the sponsor should provide explanation and justification.

Oscilloscope Tracings

For each output mode, an oscilloscope tracings (or accurate diagram) describing the electrical output waveform should be provided. For each output mode, tracings should be provided to describe the individual pulse output waveform under a 500 ohm load. Additionally, one tracing should be provided showing a series of pulses under a 500 ohm load. The following information should be included with each tracing:

- a. Name of the output mode;
- b. Clearly labeled amplitude and time axes;
- c. Identification of the amplitude baseline; and
- d. Listing of all output parameter settings (e.g., amplitude, pulse width, frequency, etc.).

Section 2: Lead(s), Electrodes and Programmer Descriptions

Lead(s)

The sponsor should identify the number of leads used with the device and describe the length, diameter, construction, materials, impedance, and connections between the stimulator device and the electrodes for each lead. The lead(s) should be compared to a legally-marketed predicate device.

Electrodes

The type and size (length and surface area) of all available and recommended electrodes should be specified. If a new material is used, biocompatibility data should be provided. If the materials are substantially equivalent to a legally-marketed electrode, the sponsor should provide identification of the legally-marketed device (including 510(k) number), and a description of similarities and differences. The number of electrodes per lead and the distance between electrodes, i.e., electrode spacing, should also be provided.

Programmer

The following information for the physician and patient (if available) programmer should be provided:

- a. Description of device and device labeling, including all buttons, switches, etc.;

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- b. Description of all outputs that are controlled (frequency, pulse width, intensity, electrodes, polarity, etc.); and
- c. Instruction manual(s).

Battery

A complete description of the battery should be provided, including life testing under worst case usage.

A discussion of whether an 'elective replacement indicator' that gives advance warning of energy source depletion causing 'end of life' of the system is included on the device. The interval between the activation of the indicator and the actual end of life of the device should be specified.

Section 3: Description of Accessories

A complete description, including illustrations if appropriate, should be provided for all device accessories including but not limited to lead blanks, lead anchors, tunneling tool, epidural needle for implantation, and magnet.

Section 4: Description of Software/Firmware/Microprocessor Control

The document entitled, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," dated May 29, 1998, provides general guidance on this subject. This guidance document may be obtained from DSMA or via the Internet at: <http://www.fda.gov/cdrh/ode/software.pdf>.

For pulse generators and test stimulators controlled by software (or firmware or a microprocessor), the following should be provided:

- a. Determination of the level of concern;
- b. Description of all device functions controlled by the software;
- c. Hazard analysis;
- d. Software functional requirements;
- e. Description of the system-level test protocol, including pass/fail criteria; and
- f. Summary of the test results.

Attachment III

Device Testing and Manufacturing

Introduction

This attachment is intended to provide guidance regarding information that should be included in a 510(k) submission for a totally implanted SCS device to document device testing and manufacturing. The documentation that should be provided includes the following:

- Section 1: *In vitro* Component Testing
- Section 2: *In vitro* Finished Device Testing
- Section 3: Environmental Testing
- Section 4: Electromagnetic Compatibility (EMC) Testing
- Section 5: Reliability Testing
- Section 6: Programmer Testing
- Section 7: Manufacturing
- Section 8: Sterilization
- Section 9: Biocompatibility

If you plan to use device testing standards, refer to the guidance document entitled, "Use of Standards in Substantial Equivalence Determinations." This guidance document may be obtained from DSMA or via the Internet at:

<http://www.fda.gov/cdrh/ode/guidance/1131.html>. In addition, if you plan to declare conformance to a standard, refer to Attachment 4 of the guidance document entitled, "The New 510(k) Paradigm, Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications." This guidance document may be obtained from DSMA or via the Internet at: <http://www.fda.gov/cdrh/ode/parad510.html>.

Section 1: *In vitro* Component Testing

Component parts, i.e., Hybrid/Integrated Circuits and/or Chip Carrier, Battery, Connector, etc., should be tested for design verification by the pulse generator manufacturer or its supplier according to written specifications of performance and testing.

The verification testing should be appropriate for the component and include appropriate operational, environmental, and reliability tests with tolerances and limits compatible with the entire system's specifications.

Section 2: In vitro Finished Device Testing

Pulse Generators

Pulse generators built for verification testing shall be representative of the marketable product in terms of components and manufacturing processes used. When completed, tests should be performed on devices manufactured from qualified components using validated processes. Where appropriate, tests should be performed on in-specification devices that have been subjected to all applicable post-process techniques, e.g., cleaning, sterilization and finishing.

Electrical Characterization

This testing should be designed to verify the proper functioning of the pulse generator within specified tolerances in the human body during the device's expected operational life. All stimulation parameters and all features must be characterized for functioning under expected temperatures (30° to 40°C), loads (300 to 2000 ohms), and battery voltage's lifetime. The device should be programmed to each mode and feature and to the lowest, nominal, and highest values of programmed parameters. Analysis of the effects of worst case combinations of load, temperature and battery voltage should be made. Testing should also be performed on the test stimulator. Any applicable portions of IEC 601-1 may be referenced.

Section 3: Environmental Testing

The pulse generator should be subjected to a sequence of mechanical and environmental tests to assure that the device will meet its labeled specifications after being subjected to conditions that exceed those normally seen in handling, shipping, storage or clinical use. Tests for hermeticity, temperature storage or cycling, mechanical vibration, and mechanical shock should be conducted. For testing involving the device as packaged, reviewing ASTM D 4332 – 99 "Standard Practice for Conditioning Containers, Packages, or Packing Components for Testing" may aid in the designing of these tests.

Section 4: Electromagnetic Compatibility (EMC) Testing

The totally implanted SCS should be evaluated for effects on its functioning and/or programming by external sources of interference. Sources of interference can be from the general environment, the clinical setting, occupational environments, or the human anatomy. These may include, as appropriate to the device design, electromagnetic, electrical, magnetic, mechanical, thermal, acoustic, or chemical interference. The effects of interference on such features as sensing, device algorithms, rate responsive sensors should be characterized. Any applicable portions of IEC 601-1-2 may be referenced.

Additional information relating to EMC is on the CDRH Home Page at <http://www.fda.gov/cdrh> by searching under "E" for Electromagnetic Compatibility in the Topic Index.

A warning describing all adverse EMC effects should be clearly stated in the labeling.

Section 5: Reliability Testing

The device should be tested and analyzed for reliability. Testing of the device or, where appropriate, its components, must include accelerated life testing that will demonstrate the expected real time longevity performance and failure rate of the device. An analysis of the testing results and/or data from the literature should result in a predicted failure rate of the device.

Section 6: Programmer Testing

Programmers built for verification testing should be representative of marketable products and subjected to functional, environmental, interference, software and reliability testing. This testing should be designed to assure its operation, according to written specifications in conjunction with any and all of its intended pulse generators, under specified, expected environmental conditions; and its survival in use, as well as in storage, shipping and handling.

Section 7: Manufacturing

Pursuant to 21 CFR 812.20(a)(3), the sponsor should provide a description of the methods, facilities and controls used for the manufacture, processing, packaging, storage in sufficient detail so that a person generally familiar with good manufacturing practices can make a knowledgeable judgment about the quality control used in the manufacture of the device. This information should be provided for both the device and its accessory components, such as, monitoring and recharging units. Pass/fail criteria for the critical steps in the manufacturing process of the device should be included.

Section 8: Sterilization

Instructions for proper sterilization of the implantable components should be provided. The sponsor should specify the sterilization method(s) used, all parameters of the sterilization cycle, sterilization assurance level (e.g., 10^{-6}), and validation of the sterilization process. Additionally, information on pyrogen and/or endotoxin content should be submitted. If the device is supplied sterile by the manufacturer, the method of sterilization, date of sterilization, lot number, date by which the device must be used, and proper steps to ensure that sterility is not compromised should be specified. Assurance that the sterilization method is compatible with the device materials should also be provided. Refer to “510(k) Sterility Review Guidance 2/12/90 (K90-1)” located on the web at <http://www.fda.gov/cdrh/k90-1.html> for further information regarding sterilization requirements.

Section 9: Biocompatibility

For patient-contacting devices, biocompatibility information and/or data for the device materials, including inks, dyes, markings, etc., should be provided. Certification that the same materials and formulations are used in the device to which you claim equivalence may be acceptable. Therefore, if the materials are identical to the legally marketed device and are

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identically processed or sterilized, this should be explicitly stated. For a material that has been tested and used in legally-marketed implanted devices, a sponsor may submit information available in publications or other sources that show that the material is nontoxic in appropriate biocompatibility tests. However, we may also request biocompatibility test results to be submitted for our review. The effects of sterilization on device materials and potential leachables, as well as toxic sterilization by-products, should be considered. Therefore, testing should be performed on the sterilized final product or representative samples of the sterilized device. Conformance to International Standard ISO-10993, "Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing" is recommended.